Comment on "Critical branching captures activity in living neural networks and maximizes the number of metastable states".

In a recent Letter, Haldemann and Beggs [1] use a branching process to simulate propagated neuronal activity in form of neuronal avalanches. This work built on an experimental paper by Beggs and Plenz [2], which demonstrated that a critical branching process captures some of the dynamics of propagation of neuronal activity through synchronized groups of neurons. Experimentally the branching parameter σ is measured as the ratio of the number of "descendant" electrodes to the number of "ancestor" electrodes activated in each avalanche. It was found in [2] that, under normal activity, cortical networks exhibit scale-free avalanches and $\sigma = 1$. In the recent Letter [1], the authors stated that the experiments reported in [2] exhibited $\sigma > 1$ during epileptic activity. This statement indicating that epileptic networks have $\sigma > 1$ is essential to the authors hypothesis and conclusions, but is false. First, the referenced paper [2] does not provide any information about the experimentally obtained branching parameter in epileptic networks and second, (as shown in Fig. 1) the branching parameter in epileptic networks is *smaller* and not larger than 1.

Fig. 1 summarizes information on cultured cortical networks including those networks used in [2], that had been made epileptic by blocking fast inhibition using the antagonist picrotoxin (PTX). As reported previously [2], networks in the critical state reveal a scale free avalanche size distribution, but when neuronal inhibition is blocked with drugs such as PTX a characteristic avalanche size appears and the distribution becames bimodal (Fig. 1A). Under these conditions, the branching parameter σ, calculated according to the formula found in [2], is significantly smaller than that for the critical state (Fig. 1B), which is in contrast to what has been stated by Haldemann and Beggs [1]. This result holds true for all three described approaches of calculating σ in these networks. Similarly, the number of significant families, i.e. the metastable states discussed in [1], is not different for the critical and epileptic state in the real cortical networks (Fig. 1C), which is, again, in contrast to the claims by Haldemann and Beggs [1].

In conclusion, the first claim in the Letter of Haldeman and Begss stating that "...the model mimicked the double peaked distribution produced when we bathed the cortical cultures in picrotoxin, an agent that selectively blocked inhibition and increased σ." is misleading. The analysis of that data shows otherwise: as seen in Fig. 1B σ *decreases*. The second claim in Haldeman and Begss indicating that cortical cultures showed increased number of metastable states is also false: as shown in Fig 1C there is no significant difference between the number of states in critical and epileptic networks.

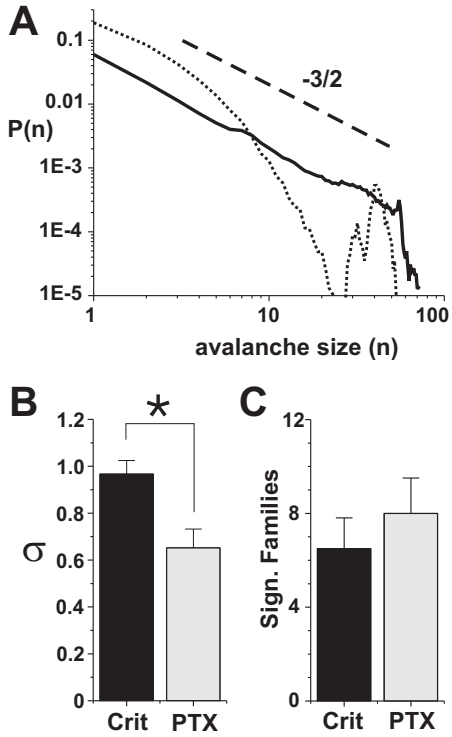

FIG. 1: Experimental estimate of branching ratio and number of different patterns in networks for two conditions: critical and made epileptic by PTX. **A.** Representative examples of avalanche size distribution in critical and epileptic networks (solid and dotted line respectively). **B.** The branching ratio $\sigma \sim 1$ in the critical state [2] ("Crit") and smaller than one in epileptic networks ("PTX") [4]. **C.**The number of metastable states is not different for critical and epileptic networks [5].

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[2] J. M. Beggs and D. Plenz. J. Neurosci. **23**, 11167-11177 (2003).

[3] J. M. Beggs and D. Plenz. J. Neurosci. **24**, 5216-5229.(2004).

[4] $\sigma = 0.97 \pm 0.15$ for critical, and 0.65 ± 0.18 for PTX networks (mean $\pm$ SEM); dF1,10 = 10.75, P = 0.008; ANOVA. Calculated from 5 PTX and 7 critical networks ($\sim$ 40,000 avalanches and 10 hrs recording per network and state).

[5] Sign. Families $= 6.49 \pm 1.3$ for critical, and 8.0 ± 1.5 for PTX networks (mean $\pm$ SEM); dF1,10 = 0.56; ANOVA; P = 0.47. Calculated from 5 PTX and 7 critical networks (1000 consecutives avalanches from each), repeated 5 times and averaged. Significance was established with 20 rate-matched shuffle sets at Type I error = 5 % as in [3].